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NASA CR-
141607

Research Report

(NASA-CR-141607) CONTINUED INVESTIGATION OF KINETIC ASPECTS OF BONE MINERAL METABOLISM Final Report, 1 Feb. 1973 - 28 Feb. 1974 (Battelle Memorial Inst.) 29 p HC $3.75 CSCL 06P G3/52

N75-17083

Unclas 09705

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Final Report of Work Completed on

CONTINUED INVESTIGATION OF KINETIC ASPECTS OF BONE MINERAL METABOLISM

Under Contract NAS 9-13235
February 1, 1973 to February 28, 1974
to the
National Aeronautics and Space Administration
Lyndon B. Johnson Space Center
Houston, Texas

by

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February 26, 1974

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CONTINUED INVESTIGATION OF KINETIC ASPECTS OF BONE MINERAL METABOLISM

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ABSTRACT

The major portion of this work was devoted to studies of the determination of total body calcium in humans by measuring expired ^{37}Ar after neutron irradiation. The excretion of ^{37}Ar from humans was found to be much slower than the excretion from rats and dogs, and seems to be related to the age of a person. This agrees with studies by other investigators of radon retention in animals containing radium, where the radon retention in the bone increased with increasing age. A study of the uniformity of the ^{37}Ar production throughout the thickness of the body was studied using phantoms. The results indicate that it should be possible to obtain a uniformity within ±3% for the production of ^{37}Ar per unit of calcium by using a bilateral irradiation. New low background, large volume proportional counters were developed, constructed and provided to the University of Washington for more sensitive measurement of ^{37}Ar in the expired air from patients.

In other studies a new irradiation enclosure was developed for measuring total body calcium in rats by the ^{37}Ar method. With this enclosure the ^{37}Ar production per gram of calcium is constant with a standard deviation of ±2.8% for any size rat between 100 and 500 grams. The use of ^{22}Na as measure of bone replacement in the fractured femur of a dog was not successful; however, there is still a sound basis that ^{22}Na or ^{85}Sr can be used to measure bone replacement in astronauts returning from space.

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PART I

STUDIES OF THE USE OF EXPIRED ^{37}Ar AS A MEASURE OF TOTAL BODY CALCIUM IN HUMANS AFTER NEUTRON IRRADIATION

Excretion of ^{37}Ar from Humans

These studies are a continuation of the studies conducted for NASA in 1972.(1) These previous studies showed that the ^{37}Ar excreted in the expired air of rats and dogs after neutron irradiation is both rapid and reproducible. The amount of ^{37}Ar, which is produced by an n, α reaction on calcium in the bone, was found to be directly proportional to the calcium content of rats and, therefore, can be used as a measure of total body calcium. The precision of the measurement was ±2% at 95% confidence for repeated measurements on the same rat and the accuracy is ±3% for the absolute calcium content in a rat of any size between 200 to 600 grams. Since the method was successful with animals, it seemed appropriate to test the method for human use since it has the potential of greater accuracy and would require only a hundreth the radiation dose presently used for neutron activation methods for total body calcium.

Although the bones of the adult human are much larger in physical size than those of the small animals, the diffusion of the ^{37}Ar out of the bone should not be limited by the larger size. Bone is a living structure which is maintained by living cells within it and by tissue fluids which move through the bone in an interlocking network of fine canaliculi. The average distance between the lines of the canaliculi is similar in the bone of both man and animals and, therefore, the diffusion of ^{37}Ar from the bone mineral to the fluids, then to the bloodstream, and finally to the lungs should be about the same for both man and animals. In previous experiments(2) the major fraction of ^{37}Ar produced in the dog, which was 30 to 50 times larger than the rats, was excreted only slightly slower than that in the rat. Since the average adult man is only about five times larger than the dog which was used, a rapid excretion of ^{37}Ar would be expected in man also.

Measurements of the ^{37}Ar excretion rate from humans were made on several patients at the University of Washington School of Medicine. These patients were being irradiated with neutrons for the purpose of determining total body calcium by measuring the induced ^{49}Ca in a whole body counter. The expired air from these patients was collected in an air bag for periods of 5 to 15 minutes at various intervals up to 5 hours. During the breath collection periods the patient inhaled a gas mixture of 70% helium and 30% oxygen. This mixture eliminated the nitrogen in the expired air except for small amounts which were dissolved in body tissues and fluids. The sample of air from the bag was slowly passed through the purification apparatus which had been developed for the animal studies. This included passing the air through soda lime to remove carbon dioxide, hot copper to remove oxygen, calcium sulfate and phosphorus pertoxide to remove water vapor, activated charcoal cooled in liquid nitrogen to collect all ^{37}Ar, and the helium passed on through to the atmosphere. Details of this gas separation procedure are given in the previous final report for the 1972 studies.(1)

The activated charcoal traps containing the ^{37}Ar from the air samples were then transported to the Battelle Laboratories at Richland, Washington, for further processing and counting since the University of Washington was still in the process of setting up apparatus and instrumentation to measure the samples.

The ^{37}Ar excretion rates from two patients are shown in Figure 1. Additional patients have been measured, but the entire procedure was conducted at the University of Washington, and those results will be published in their final report. The results from the first two patients are typical of the results obtained on the other patients. The ^{37}Ar excretion in both patients is significantly slower than that measured in dogs and rats. In the 63-year old female patient, who was being treated for osteoporosis, the excretion rate at 5 hours after irradiation is still more than 10% of the rate immediately after irradiation, and the rate appears to be falling off slowly. The ^{37}Ar excretion from a younger

37-year old male patient was somewhat faster but both results indicate a component of excretion exists which has a half-time of many hours.

The expired air collections from these two patients were started 2 minutes after the end of a 1 minute irradiation, which left a question whether a very rapid component of excretion was being lost during the 3-minute period. Subsequent measurements have included measurements of air expired during and immediately after neutron irradiation. The excretion rate of ^{37}Ar during the period, including the 1-minute irradiation and 2 minutes after irradiation, was only two-thirds that of a similar collection period starting 2 minutes after irradiation. This indicates that the release of ^{37}Ar is limited by the diffusion out of the bone into the blood. The half-time of noble gases in the blood is known to be only several seconds, so apparently the diffusion of ^{37}Ar from the bone is quite slow and, therefore, it takes several minutes for the maximum excretion rate to occur in the expired air. Possible reasons for this slow diffusion from the bone will be discussed in the next section.

Comparison of ^{37}Ar Excretion from Humans, Dogs, and Rats, and Also With Age

The results of studies conducted at the University of Utah[3,4] of the radon retention in dogs and mice containing ^{226}Ra deposited in the bone help to explain the differences in the excretion rates of ^{37}Ar we have observed in humans and animals. These studies show that the radon retention increases with age of the bone and the increased retention with age is about the same for mice, dogs and man. This means that a 1-year old man, mouse, and dog would have the same retention but a 70-year old man would have a higher retention than a 10-year old dog, which would exceed that in a 2-year old mouse. Our results from ^{37}Ar formed in the bone agree very well with the radon retention results and Figure 2 shows that the retention of ^{37}Ar in the 63-year old woman is greater than that in an 18-month old dog, which in turn is greater than that in a 3-month old rat. Also, Figure 1 shows the retention in the 63-year old woman is greater than that of a 37-year old man.

In the 3-month old rat, we found a very rapid excretion of ^{37}Ar[1], such that more than 99% of the ^{37}Ar appeared to leave the body within 2 hours and there was no apparent long-term component of excretion. Subsequent measurements on a 6-month old rat showed a somewhat slower excretion and the data is listed in Table 1. In the second hour after irradiation, 2.6% of the expired ^{37}Ar was excreted and an additional 1.1% was excreted during the third hour. The retention of ^{37}Ar during the second and third hours is significantly higher than that in the 3-month old rat.

In addition to that found in the expired air, some ^{37}Ar still remained in the bones. At 4 hours after irradiation the 6-month old rat was sacrificed and the femur and tibia bones were removed and dissolved in nitric acid. The off gases were collected and the ^{37}Ar content from these bones were measured. From these results the total ^{37}Ar remaining in the entire skeleton was estimated. By adding this amount to the expired ^{37}Ar it was determined that 88.6% was excreted in the first hour, 2.5% in the second hour, and 1.0% in the third hour, and at 4 hours after irradiation 7.9% still remained in the rat and was being excreted at a rather low rate. These results show that the ^{37}Ar excretion is age dependent even in quite young rats.

The investigators in the radon retention versus age studies[3,4] have postulated that the higher retention with increasing age is due to the increase in mineral fraction in the older bone and an enlargement of the bone crystals which, in turn, reduces the ability of the radon to diffuse out of the bone. If this is true then this same condition undoubtedly affects the excretion rate of ^{37}Ar from the bone.

<u>Estimation of the Fraction of Total ^{37}Ar Expired From 63-Year Old Human During First 5 Hours After Irradiation</u>

The excretion rate of ^{37}Ar from a mature but young beagle dog (18 months old) has been studied in detail.[2] Ninety-five percent leaves the dog with a half-time of 15 minutes, another 3.9% leaves with a half-time of 5.8 hours, and the remaining 1% leaves with a half-time of 7 days. This same dog was irradiated with neutrons at the University of Washington Cyclotron under the same conditions used for patient irradiation. From bone mineral studies in beagle dogs[5] the calcium content of the dog was estimated to be about 100 grams. After counting ^{37}Ar in the expired air from the dog, the counts per minute of ^{37}Ar formed in the dog per gram calcium per rad of dose was calculated to be 2.0. Assuming the 63-year old patient, whose results are shown in Figure 1, has about 800 grams of calcium and by integrating the counting rate of all the expired ^{37}Ar during the first 5 hours, the count per minute per gram of calcium per rad comes out to be 0.69. When compared to the dog results, this suggests that only 0.69x100/2 or about 35% of the total ^{37}Ar has left the body within the first 5 hours, and 65% either remains in the body or has escaped through the skin. It seems unlikely that a significant amount of ^{37}Ar would escape through the skin of a person since it is so readily released into the lungs from the blood. Therefore, this rather large fraction of the total ^{37}Ar appears to still remain in the body and is excreted very slowly for many hours or possibly a few days. This method of estimation, by comparing the ^{37}Ar excretion with a dog, is not a precise measurement and could be off by ±30%.

The Uniformity of ^{37}Ar Production Throughout the Thickness of the Human Body

The neutron cross section for the reaction ^{40}Ca (n,α) ^{37}Ar is 138 millibarns at a neutron energy of 14 MeV. The cross section increases as the neutron energy decreases and at 6 MeV it is 430 millibarns. At lower energies, the cross section decreases. Unfortunately, there is no available experimental data on cross section values between 6 and 14 MeV, so that the peak cross section value is unknown. When a neutron beam passes through a thickness of water, both the average energy and the number of neutrons are reduced by thermalization and capture. In the case of the activation of ^{40}Ca to produce ^{37}Ar, the loss of neutrons by absorption with greater penetration into the body is somewhat compensated by the higher cross section of reaction for the remaining lower energy neutrons. Because of this effect, the uniformity of the activation of the ^{40}Ca by a beam of fast neutrons should be greater than that of a reaction in which the cross section becomes lower as the neutron energy is reduced.

A study was conducted to determine the uniformity of ^{37}Ar production throughout the thickness of the body. These studies were done using a water phantom 11 in. thick, 18 in. high and 18 in. wide. The larger width and height were used so that the calcium activation at various depths within the 11 in. thickness would not be affected by the neutron escape from the sides, top, or the bottom of the phantom. A tube containing a calcium nitrate solution, with helium continuously bubbling through it, was placed at various distances from the face of the 11 in. thickness in the center of the height and width dimensions of the phantom. The ^{37}Ar produced during neutron irradiation is released to the stream of helium and collected on cold activated charcoal for subsequent measurement. The release of ^{37}Ar from the calcium solutions is not immediate and 2 hours are required for the stream of helium to remove 99% of the ^{37}Ar from the solution.

Figure 3 shows the relative amount of ^{37}Ar produced from a constant amount of calcium undergoing a constant amount of neutron irradiation at various positions from the surface of the 11 in. thick water phantom. The curve is nearly straight. Since, in actual practice, the patient will be irradiated from both the front and the back, the two curves can be added to obtain a bilateral summation curve which is nearly straight and horizontal within ±2.6%. Since the thickness of most people can be easily compressed to 11 in. or less, and thinner sections of the body can be covered with water to produce an effective constant 11 in. thickness over the entire length of the body, it should be possible to equally activate the calcium in the human body within ±2.6%, regardless of its position within the body.

The Development of a Low Background ^{37}Ar Proportional Counter

The proportional counter used for measuring the ^{37}Ar activity for animal experiments has been described in detail in the report on the 1972 studies.[1] The volume of that counter is 113 cm^3 and the background under the 2.82 keV photopeak is about 2 counts per min. This counter was also used to count the ^{37}Ar activity in the expired air fractions of most of the patient studies during 1973. A larger volume counter is required for counting the entire sample of expired air from humans since the stable argon, which comes from that dissolved in the patient's tissues, is estimated to be about 200 cm^3, and an additional amount results from the stable argon, which exists as a contaminant in the helium-oxygen mixture which the patient breathes. The background of the counter also needs to be reduced so that long counts on the ^{37}Ar can be made on samples of low ^{37}Ar content, which will result when radiation dose to the patient or astronaut is reduced to just a few millirad.

The two primary methods for reducing the background of proportional counters are (1) the use of very pure construction materials to eliminate radioactivity in the walls of the counter, and (2) the use of anticoincidence shielding, which discriminates against the pulses in the counter which are produced by cosmic ray events. After studying some of the techniques used at the National Bureau of Standards for the construction of counters for measuring ^{37}Ar in the atmosphere,[6] two counters were constructed for use in measuring expired air samples from humans. One counter was constructed from Delrin plastic and the other of quartz and both counters were lined with ultra-pure aluminum foil to act as a cathode.

The Delrin plastic counter was 25.4 cm long, and had an inside diameter of 5.08 cm which gives a volume of 514 cm^3. The inside of the Delrin tube was first lined with a grid of 0.0058 cm diam stainless steel wires at a spacing of one-eighth inch which formed the cathode of the counter. The anode was a 0.0025 cm diam stainless steel wire through the center of the tube. The ends of the counter, the tube, the anode, and cathode wires were held in position by a low vapor pressure epoxy (Torr Seal).

The counter was outgassed for several days under vacuum and then filled with 90% Argon - 10% methane counting gas. The resulting background was dissappointing at 5 counts per minute. The stainless steel wire grid cathode was replaced with a 0.0058 cm thick sheet of zone refined aluminum which had a purity of 99.9995%. The background dropped to 0.8 count per min, which is a factor of 12 lower than that obtained with the old counter when considering the larger volume of this Delrin counter. The resolution of this counter was not as good as it should be, which may be due to outgassing of impurities from the Delrin counter material into the counting gas.

The quartz counter was made from commercial grade quartz tubing 4.60 cm in inside diameter and 24.1 cm long, which provided a volume of 401 cm^3. A diagram of the counter is shown in Figure 4. The inside of the tube was lined with the ultra-pure aluminum described in the previous paragraph. A stainless steel 0.0025 cm wire was used as the anode. The counter was cemented together with a low vapor pressure epoxy (Torr Seal). The background of this counter was 0.3 counts per minute under the 2.82 keV photopeak from ^{37}Ar, and the photopeak had excellent resolution. This is significantly better than the Delrin counter described above and is adequate for counting ^{37}Ar in the expired air samples from humans after low levels of neutron irradiation. This background is obtained with the counter between two 24 cm diam by 10 cm thick NaI(Tl) detectors which act as an anticoincidence shield for the cosmic ray events and this whole assembly is shielded by 10 cm thickness of lead. If it becomes necessary, the background of this type of counter can probably be further reduced by using pulse shape discrimination to further reduce the cosmic ray contribution to the background and by using an extremely pure grade of quartz tubing which is made from zone refined silicon which is then converted to quartz. However, this grade of quartz is very expensive.

The two counters described above have been given to the University of Washington School of Medicine for their use in studying the method of determining total body calcium in patients by measuring expired ^{37}Ar after neutron irradiation.

Consultation Provided to the University of Washington

Consultation was provided to the University on the design and construction of apparatus for collecting expired air from human patients and processing and purifying the samples prior to the ^{37}Ar measurement. The procedures used for the human studies are the same as those used for the animal studies but are done on a larger scale. One major difference will be that the breathing gas mixture of helium and oxygen will be continuously recycled with the extraction of CO_2 and water vapor, and the addition of oxygen as needed; whereas, in the animal studies the gas mixture flowed through the breathing chamber only once. The air recycling apparatus was developed by University of Washington personnel and will result in a great saving in the amount of helium and oxygen gas mixture used. The small amount of this gas mixture required for animal studies did not justify using a recycle system.

Consultation and suggestions were also given for the construction of their irradiation facility which will use a neutron generator similar to that used in the animal experiments.

Summary and Recommendations for ^{37}Ar Studies in Humans

The advantages of the ^{37}Ar method for total body calcium measurements over existing methods using neutron activation include: (A) a much lower irradiation dose; (B) fewer and less expensive facilities and equipment; and (C) possible improved accuracy. The neutron radiation dose to a human should be only a few millirads or one-hundredth of that currently required in present methods. The ^{37}Ar method does not require an expensive whole-body counter, and the neutrons can be supplied from relatively inexpensive sources such as neutron generators, α,n type, or ^{252}Cf sources. Because ^{37}Ar has a half-life of 35.1 days, the precision timing required for the 8.8-minute half-life ^{49}Ca method is not necessary, and the fluctuations in beam current during irradiation do not affect the accuracy of the method. The accuracy of this ^{37}Ar method could be better than the whole-body counting methods because there are no radioactive interferences in the separated ^{37}Ar once the short-lived ^{41}Ar has decayed away, and counting errors due to geometry and self-absorption due to various body sizes are eliminated. Studies of the uniformity of a bilateral irradiation of calcium sources in a water phantom indicate that the uniformity of the reaction $^{40}Ca(n,\alpha)^{37}Ar$ throughout the body should be within ±2.6% in adult human patients. Such uniformity is better than that which is presently being obtained in total-body calcium methods.

In humans, this method could be very useful in studying and assessing bone disease and in studying the apparent calcium loss in astronauts during space travel. However, it is evident that the slow excretion of the ^{37}Ar from humans may limit the usefulness of this method because it may not be practical to collect expired air for the many hours required for it to leave the body. This decision rests with the physicians working on this study and it is recommended that the studies on this method should be continued until they have enough information to make this decision. If the method does not turn out to be successful because of the slow ^{37}Ar excretion, the effect of slower excretion with increasing age may be used to measure the quality of the bone in the skeleton.

TABLE 1. Excretion of ^{37}Ar in the Expired Air of a Six-Month Old Rat

Time Interval Since 1 Minute Long Irradiation	Percent of Total Expired ^{37}Ar	Accumulative Percent ^{37}Ar
0 - 15 min	85.3	85.3
15 - 30	7.4	92.7
30 - 45	2.0	94.7
45 - 60	1.1	95.8
60 - 120	2.6	98.4
120 - 180	1.1	100.0

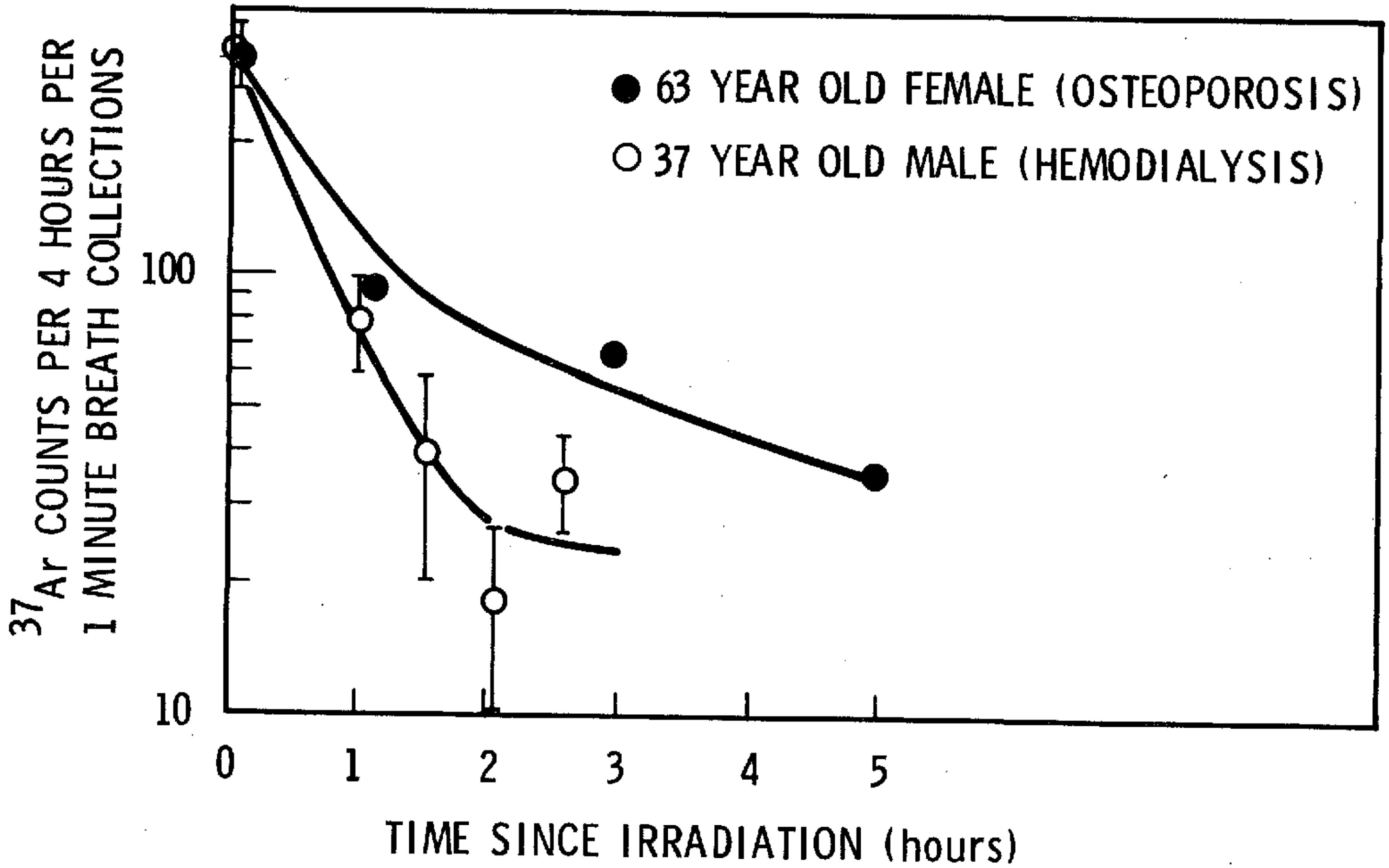

FIGURE 1. Excretion Rate of ^{37}Ar in Expired Air From Patients After Neutron Irradiation

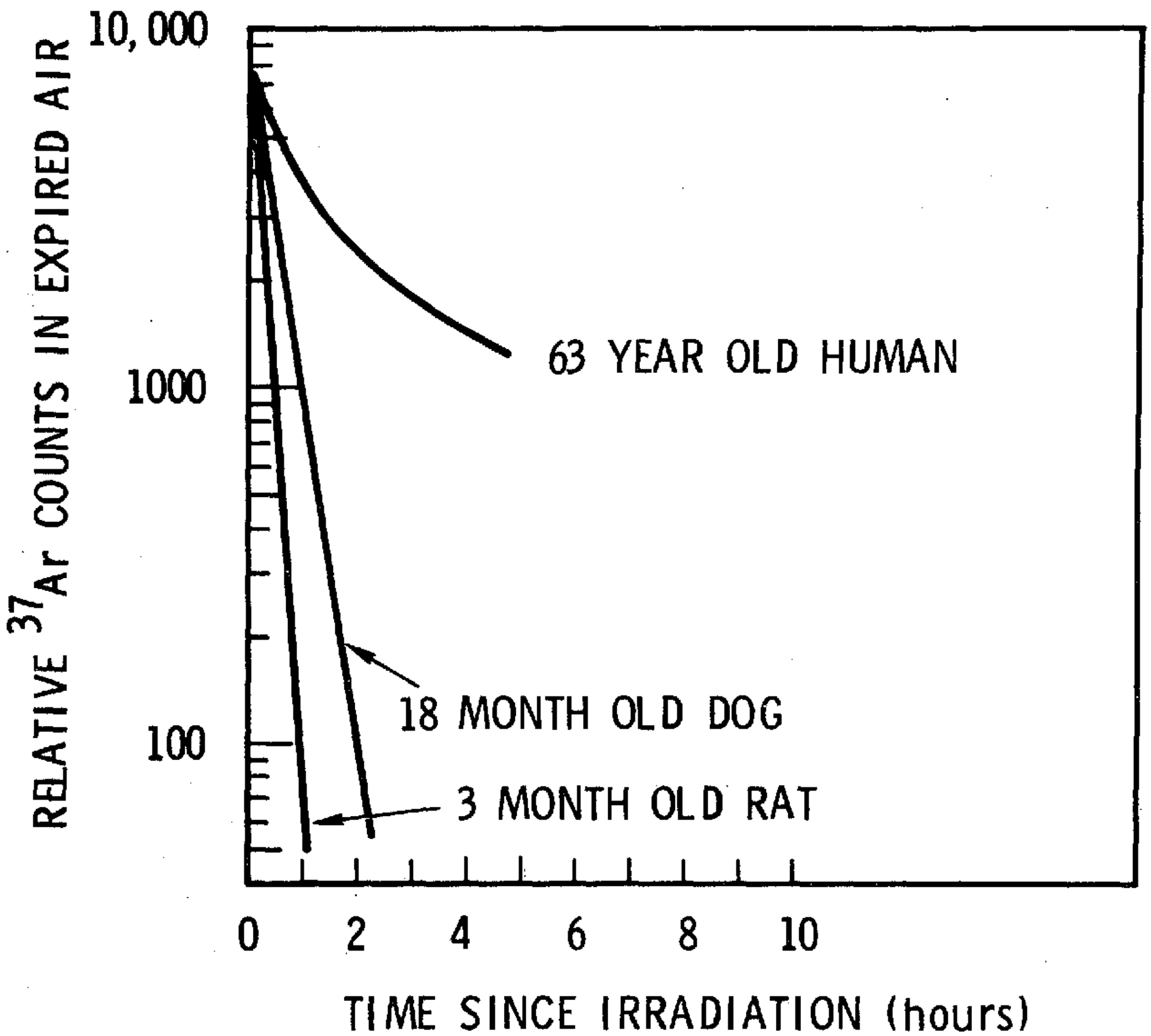

FIGURE 2. Comparison of ^{37}Ar Excretion Rates From Man, Rat and Dog After Neutron Irradiation (All Counts Normalized to the Initial Measurement)

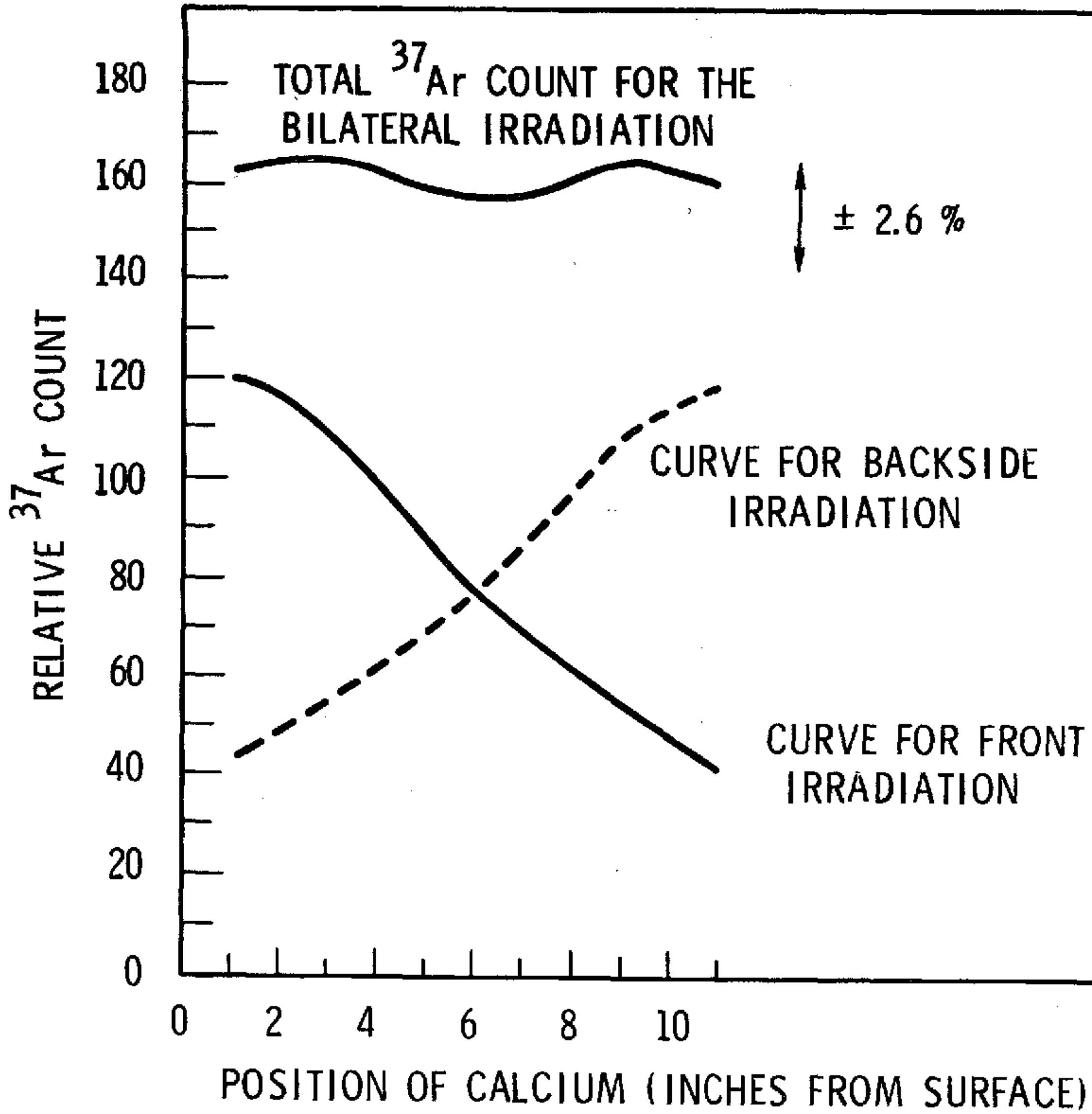

FIGURE 3. Uniformity of ^{37}Ar Production in 11-Inch Thick Water Phantom

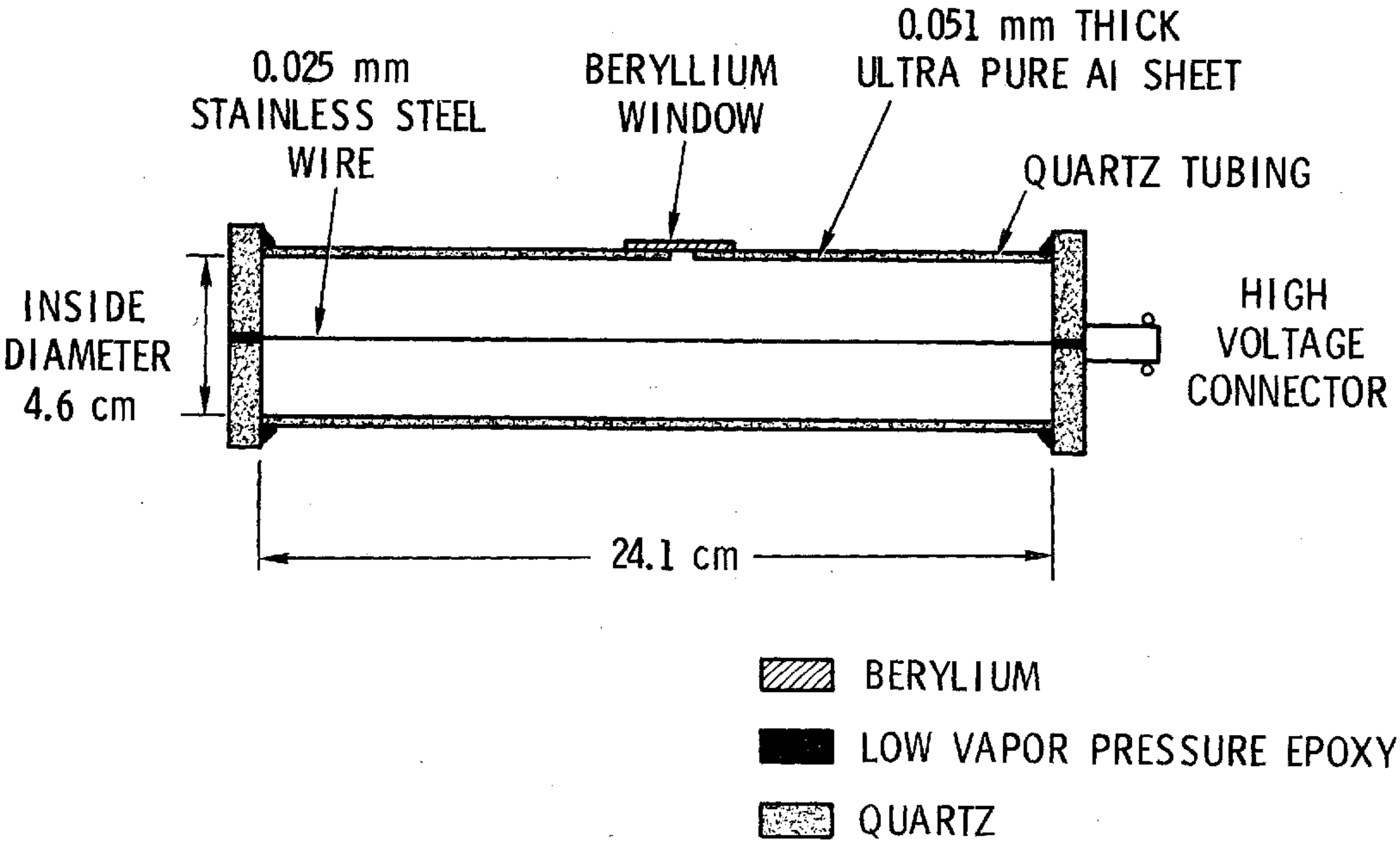

FIGURE 4. Low Background Proportional Counter for ^{37}Ar Counting

PART II

FURTHER STUDIES OF TOTAL CALCIUM DETERMINATION IN RATS BY MEASURING EXPIRED ^{37}Ar

Development of a Method for Rats Which is Independent of Body Size

At the end of the 1972 studies[1] an experiment was in progress in which the ratio of ^{37}Ar per gram of total body calcium was being measured in six different size rats ranging from 205 to 590 grams. The rats were irradiated within a specially designed block of paraffin in which the increasing size of the rat displaced some of the paraffin and, therefore, all parts of the body would be uniformly irradiated with neutrons. After duplicate irradiations and ^{37}Ar measurements, the rats were sacrificed and the total body calcium was determined by chemical analysis. The results of these studies were completed after the final report was written. They showed that the ^{37}Ar per gram was not quite constant but decreased with increasing body weight. This ratio decreased 20% between the 205 gram and the 590 rats, however, the points for all other rats fell within ±2% of the line drawn between the points of the rats.

We had hoped that the ^{37}Ar per gram of calcium would be completely independent of body size and still felt that this could be accomplished. The decrease in ^{37}Ar to calcium ratio with increasing body size was probably due to the fact that polyethelene was used as the block of moderator, whereas, the rat's body is mostly water. The hydrogen content of water is 26% less than polyethelene, so that where a larger rat displaces some polyethelene, less neutron moderation occurs and less ^{37}Ar per gram of calcium is produced. A new experiment was conducted in which all the parts of the paraffin moderator block were replaced by water. A drawing of this new irradiation facility is shown in Figure 5. The upper adjustable water filled piston compresses the living rat into a rather compact cylinder so that its body is an extension of water moderator. The rat receives half the neutron irradiation in one position, then the cylinder containing the rat is rotated 180 degrees and then exposed to the other half of the irradiation.

The ^{37}Ar was measured in duplicate on ten rats after neutron irradiation in this facility. The ten rats ranged in body size from 100 to 484 grams. The rats were ashed and analyzed for total body calcium by atomic absorbtion spectrometry. The ratio of ^{37}Ar to calcium is plotted against the weight of the rat in Figure 6. The ratio is constant with a standard deviation of ±2.8% for all body sizes in this range. The variation could be in the chemical analysis of the calcium as much as the ^{37}Ar measurement.

It appears that the precision of ±2% for measuring the same rat and an absolute accuracy of about ±3% for a rat of any size is the best we can do by the present procedure. This sensitivity for changes in total body calcium in rats is sufficient for measuring significant losses of total body calcium during space flight, if the need arises. The method accuracy could undoubtedly be improved with more development and testing; but due to the low priority for animal studies, this will conclude our efforts in this direction.

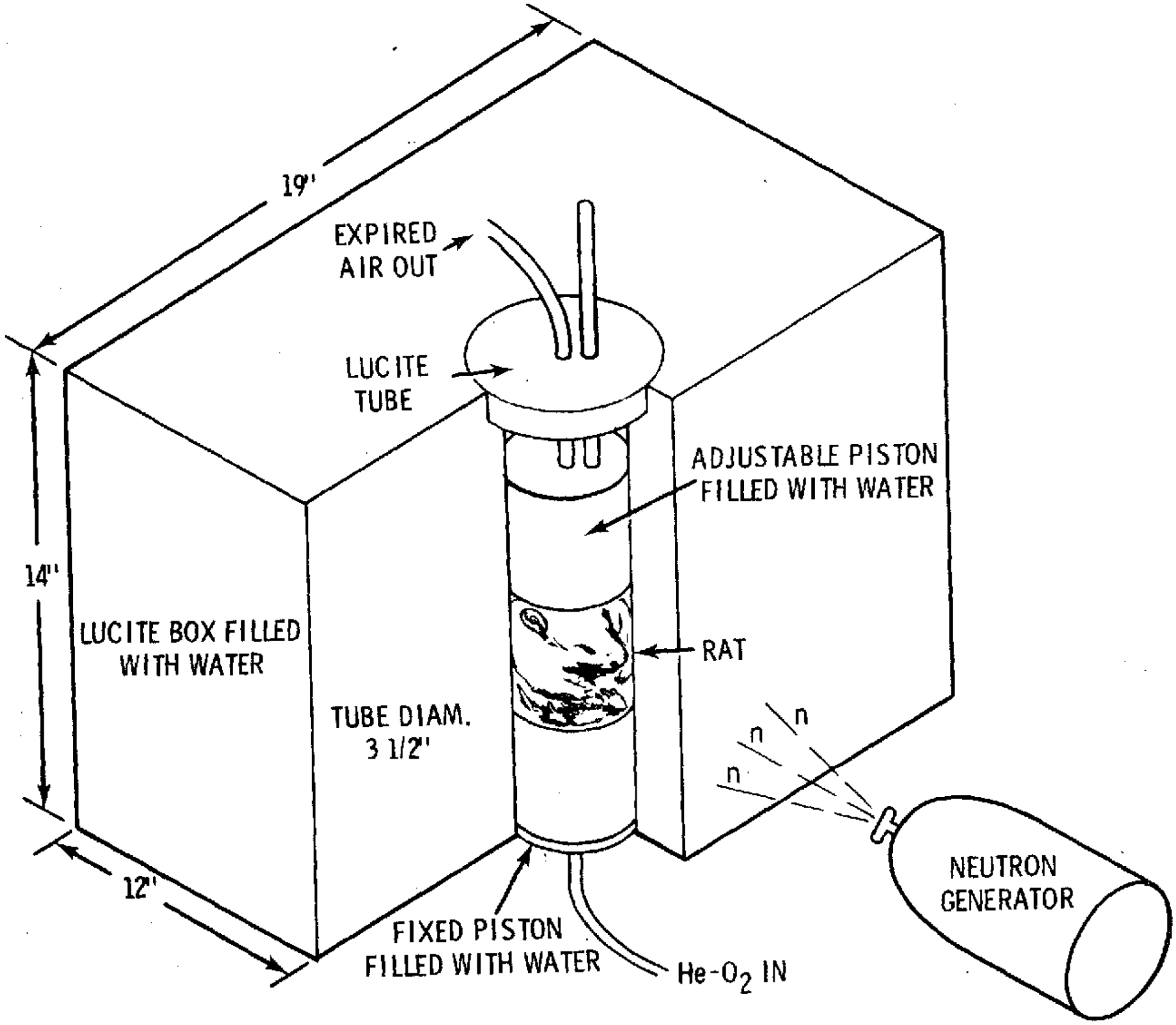

FIGURE 5. Neutron Irradiation Facility for Rats In Determining Calcium From Expired ^{37}Ar

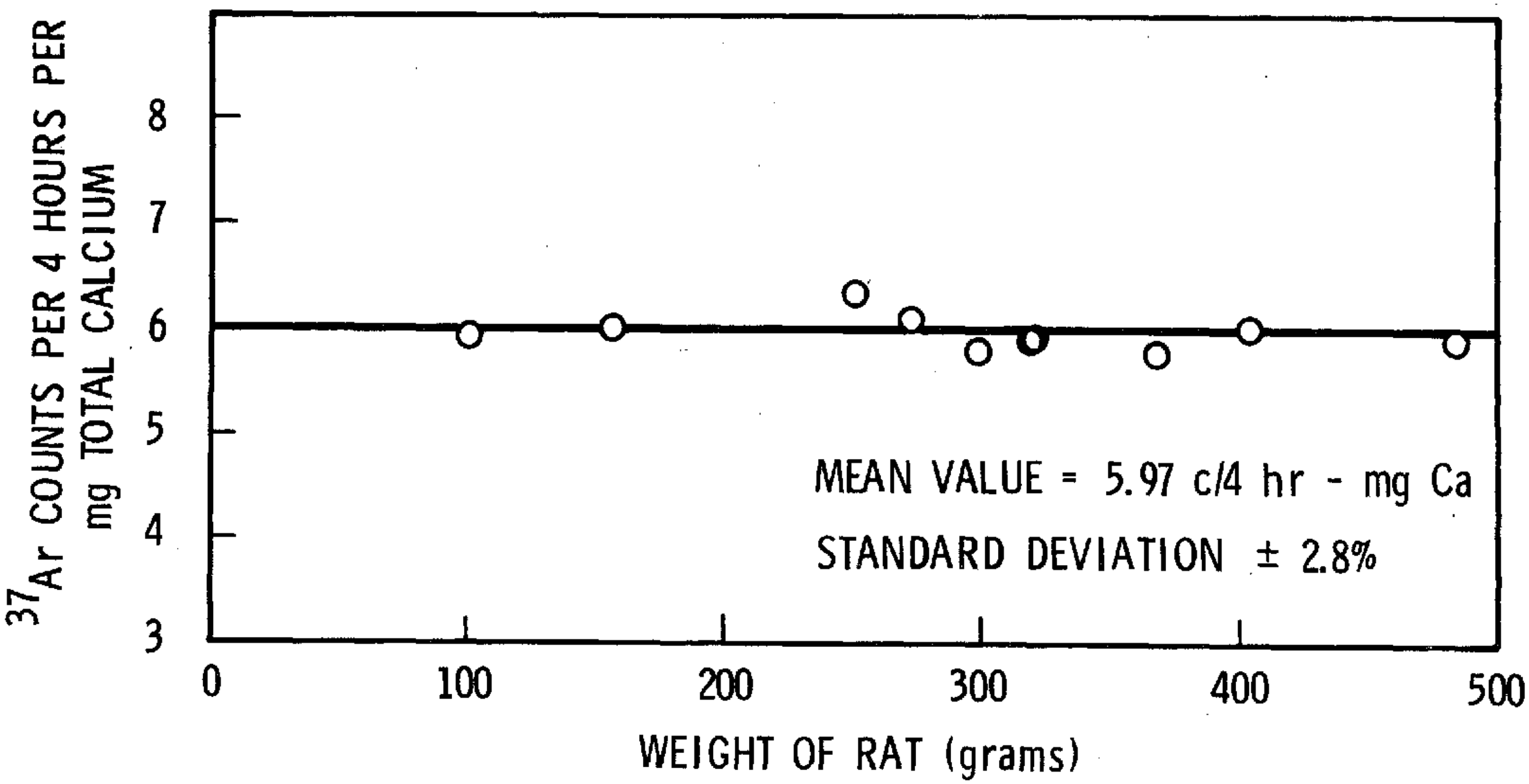

FIGURE 6. The Production of ^{37}Ar per mg Calcium Versus Body Size of Rats After Being Irradiated With Neutrons in a Water Moderated Exposure Chamber

PART III

A STUDY OF THE USE OF RADIOISOTOPES IN MEASURING REPLACEMENT BONE MASS AFTER SPACE FLIGHT

A suggestion was presented in the final report of the 1972 studies(1) that, instead of attempting to measure the bone mass loss in an astronaut during space flight, it might be easier to measure the replacement bone mass which occurs after space flight. To do this, immediately upon return to earth an astronaut would be given a small amount of radioactive isotope of an element which is located mostly in the bone. The body burden of the isotope would be maintained relatively constant during the few weeks in which the bone replacement occurs. After this time, the isotope would be allowed to leave the soft tissues and fluids until the major fraction is found only in the skeleton. At this time the body could be scanned for radioactivity and the areas of bone replacement would be more radioactive than bone which had undergone normal mineral turnover. From this scan both the place and the amount of the bone mass replacement could be determined.

Calcium, phosphorus, strontium and sodium isotopes are elements which form the bone mineral. Calcium isotopes are either too short lived for this experiment or do not have appropriate gamma ray energies for scanning. The only long-lived phosphorus isotope, ^{32}P, does not emit any gamma rays. ^{85}Sr and ^{22}Na are possible candidates since they have a long half-life and both emit 0.51 MeV gamma rays. The biological half-life in soft tissues is 2.8 days for ^{85}Sr and 11 days for ^{22}Na. Therefore, ^{85}Sr is probably the best choice since scanning of the skeleton could be done much sooner after the bone replacement has occurred.

Two preliminary animal experiments were tried with ^{22}Na to test the bone replacement measurement concept. However, both experiments were unsuccessful and are only briefly described. In one experiment, three rats were made calcium deficient by the feeding of a non-calcium diet during pregnancy and lactation periods. ^{22}Na was then injected at the same time the rat was started on a calcium adequate diet to provide calcium for bone mineral replacement. The three rats were quite uncooperative in that one refused to become pregnant, another either ate or killed her entire litter, and the third mysteriously lost her injected dose of ^{22}Na with a half-life of one day rather than the expected 10 days. In the other experiment, two ribs of a dog were broken by surgery and then allowed to heal during which time the ^{22}Na content was kept constant. No observable callus formation resulted at the fracture points and no increased amount of ^{22}Na could be detected at those positions after the ^{22}Na had been excreted from the soft tissues and fluids. The femur of the dog was then broken, pinned, and allowed to heal. Again, no significant callus formed and no increase in ^{22}Na could be observed at the point of fracture. Neither of these experiments were helpful in determining if the bone replacement method will work on astronauts returning from space travel. The type of bone mass loss experience by astronauts in space probably cannot be duplicated in animal experiments and, therefore, any further experiments should be done on bed rest patients or astronauts themselves.

To illustrate the possible potential of this method the following theoretical example is given. As a starting point, assume that:

(1) During space flight an astronaut loses 15% of the bone mineral in the os calcis, 10% in a lower vertebra and 1% in the radius. The total body bone mineral loss was 2%, and

(2) Within 14 days after return to earth, 90% of the bone mineral loss is replaced by natural repair.

Then immediately upon return from a space flight, the astronaut is given, by ingestion or injection, a very small amount of ^{85}Sr which has a 65 day half-life and is incorporated into bone in a way identical to calcium. Every other day he is given an added amount to keep the ^{85}Sr level in the body reasonably constant for 14 days. After the fourteenth day the ^{85}Sr leaves the soft tissues of the body with a half-life of 2.8 days so that after an additional 3 weeks only 0.1% of the original ^{85}Sr remains in the soft tissues, but the bone contains roughly 30% of that originally in the soft tissues. A differential scan of the astronaut will show "hot spots" where the replacement bone mineral has incorporated larger amounts of ^{85}Sr. The relative ^{85}Sr counts over the os calcis, lower vertebra, radius and total body of the astronaut are compared with those of a control subject who had not been in space, but had gone through the same post-flight ^{85}Sr administration procedure.

The data in Table II were estimated from well established metabolic data of ^{85}Sr in humans and shows the potential sensitivity of the method. This sensitivity cannot be approached by bone mineral loss measurements because in those methods we are trying to see the small difference in two large numbers, whereas, with this method we would be measuring the difference between the normal bone replacement, which is very slow, and the replacement due to space travel, which can be very much larger. As may be seen in the case of the radius, even a 1% bone loss would result in a count 2.4 times higher than the normal bone turnover rate and the 15% loss in the os calcis would result in a count 21 times higher than normal. The quantitative amounts of bone mineral lost in specific bones and the total body can also be determined from the ^{85}Sr counts.

For the astronaut the measurement procedure would be relatively simple. He would receive a capsule or injection every other day for 2 weeks; then, after 5 weeks he would be counted for 2 or 3 hours. The radiation dose resulting from the intake of ^{85}Sr would be a few millirems or less than one-hundreth that required for <u>in vivo</u> neutron activation analysis. The instrumentation needed for counting in this procedure is much less than that needed for <u>in vivo</u> neutron activation analysis and is available in the underground whole body counter at the Johnson Space Center.

In order to determine if this bone replacement measurement will work, experiments should first be performed to determine the normal uptake of ^{85}Sr in the various parts of the skeleton in normal subjects.

The next step would be to do the same experiment on those subjects just finishing their term of bed rest in NASA sponsored bed-rest studies. If the bed-rest experiments were to give encouraging results the method could then be used on returning astronauts.

TABLE II. Hypothetical Comparison of ^{85}Sr Counts in Various Bones of an Astronaut After Space Travel and a Control Subject

	^{85}Sr Counts			
	Os Calcis	Lower Vertebrae	2" Section of Radius	Total Body
Astronaut	1498	1001	169	7700
Control Subject	70	70	70	2000

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